

AMENDMENTS

In the Specification:

Please amend the specification at page 5-6 as follows:

Based on the large number of GPCR family members and the prominent role in regulating cellular signals, GPCRs represent the most important family of drug targets. The following methods are available to study interaction of potential ligands with GPCRs: a. Ligand-binding assay: This method is restricted to available radio- or fluorescent-labelled ligands, which limits its use to known receptors. Based on the nature of this assay, just the interaction of the ligand with the receptor can be studied but no information regarding the activating, blocking- or inhibiting properties of the ligand on the receptor can be gathered. b. Recording of the activity of G-protein effector systems has become the most important method for drug screening of GPCRs. (Milligan G & Rees S; Trends Pharmacol Sci. 1999 Mar;20(3):118-24.) To measure the activity of G-protein effectors makes high-throughput screening on cell based assays possible, however because of the fact that the effector system is several steps downstream of the receptor activation this method has following disadvantages: 1. It is prone to unspecific drug effects, that are not mediated via the investigated GPCR, but rather result from either interaction with elements of the signalling cascade that are downstream of GPCRs or are mediated in parallel via other (endogenous) GPCRs of which many kind are present in various cell systems (world wide web at [\[\[http://www.tumor-gene.org/GPCR/gpcr.html\]\]](http://www.tumor-gene.org/GPCR/gpcr.html)). 2. Receptor activation and deactivation cannot be determined in real time. Therefore, it is impossible to distinguish between receptor activation and fast receptor desensitization. 3. Recording of GPCR activity depends on expression levels and specificity of subsequent G-proteins and effectors, preventing in many cases exact comparisons between different GPCR subtypes. 4. The strength of the signal or the potency of a ligand to induce full activation of a cellular signal will largely depend on the expression level of the receptor (Bünemann et al. J Biol Chem. 2001 Dec 14;276(50):47512-7.). Uncontrolled fluctuations of the expression level will cause variability of the result, and will again make comparisons between different GPCR subtypes difficult. 5. A possibility to measure agonism, partial agonism, inverse agonism and neutral antagonism on the level of the receptor is lacking.

Please amend the specification at page 46 as follows:

~~The Figures show:~~ Brief Description of the Drawings